IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Suffin et al.
Serial No.: 10/697,497 Art Unit: 1617
Filed: 10/30/2003 Examiner: Kim, J.
Entitled: **Compositions and Methods for Treatment of Nervous System Disorders**

DECLARATION OF DR. STEVEN SUFFIN UNDER 37 CFR § 1.132

Mail Stop –Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Dated: July 23, 2007 By: Traci E. Light

Examiner Joyce:

I, Steven Suffin, M.D. under penalty of perjury, state that:

1. I am one inventor of the embodiments of the invention as claimed in the United States patent application captioned above.

2. I am qualified as an expert in the field of psychiatry and electrophysiological functioning of the brain.

3. I understand that, in the Final Office Action dated January 1, 2007 the Examiner believes that oxcarbazepine can be routinely substituted for lamotrigine because both drugs are classified as sodium channel blockers as suggested in Quessy et al., United States Patent Application Publication No. 2002/0147196.

4. I now provide data showing that lamotrigine and oxcarbazepine do not have similar effects on brain electrophysiology. Chart 6.1 and Chart 6.2 presents normalized Z scores showing the effect of lamotrigine (blue bars) and oxcarbazepine (red bars) on sixty-four (64) rEEG multivariate measurements. Thirty-two (32) of the rEEG multivariate measurements (50%) responded to the two drugs in qualitatively opposite directions. Eleven (11) of the remaining thirty-two (32) rEEG multivariate measurements, while having qualitatively similar responses, differed in magnitude by at least a two-fold difference. Consequently, forty-three (43) of the sixty-four (64) measured rEEG multivariables (i.e., approximately 67%) demonstrated significantly different responses when comparing the effects of lamotrigine to those of oxcarbazepine.

5. Chart 6.1 and 6.2 were assembled by calculating Z scores from response distribution patterns using individual patient data. These differential response patterns between lamotrigine and oxcarbazepine is consistent with our baseline data showing that lamotrigine has rEEG patterns consistent with stimulant drugs while oxcarbazepine has rEEG patterns consistent with depressant drugs. For example, an overall pattern of responses for the rEEG multivariable RPMZPT to several different stimulants are shown in Chart 1, while an overall pattern of responses for the RPMZPT multivariable to several different depressants are shown in Chart 2. Chart 3 (lamotrigine) is easily determined as matching the distribution for stimulants (Chart 1), while Chart 4 (oxcarbazepine) is easily determined as matching the distribution of depressants (Chart 2).

6. The above opposite rEEG effects of lamotrigine and oxcarbazepine were confirmed in trials where pre-drug rEEG measurements were compared to post-drug rEEG measurement in the same individuals (i.e., pair-wise comparisons). Table 1 and Table 2 present data for four (4) different rEEG mulivariates showing opposite effects of lamotrigine and oxcarbazepine.

7. In conclusion, these data show that lamotrigine and oxcarbazepine are not interchangeable simply because they have been suggested to have a mechanism of action in common (i.e., for example, sodium channel inhibition).

Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Dated: July 20, 2007

Stephen Suffin, M.D.